Volume 12 • Number 3 • 2009
VALUE IN HEALTH

ISPOR Fourteenth Annual International Meeting Research Abstracts

PODIUM SESSION I: HEALTH CARE DECISION-MAKER'S CASE STUDIES I

CASE1

LESSONS LEARNED: FROM COVERAGE WITH EVIDENCE DEVELOPMENT FOR POSITRON EMISSION TOMOGRAPHY SCANS FOR ONCOLOGIC INDICATIONS

Whicher DM, Tunis S
Center for Medical Technology Policy, Baltimore, MD, USA

ORGANIZATION: The Centers for Medicare and Medicaid Services (CMS). **PROBLEM OR ISSUE ADDRESSED:** In 2005, CMS issued a national coverage determination for Positron Emission Tomography (PET) for oncologic indications not previously covered by Medicare, which provided payment for PET scans for these indications only in the context of an approved prospective clinical trial designed to assess clinical utility of PET. CMS instated this policy option, referred to as 'Coverage with Evidence Development' (CED), due to the lack of evidence demonstrating the clinical effectiveness of PET scans for patient management, which is necessary to determine whether PET scans are reasonable and necessary for the diagnosis, staging, re-staging, and monitoring of various cancer types. CED allowed CMS to guide evidence development while providing access to this potentially beneficial technology. **GOALS:** To determine whether PET imaging is clinically effective for previously uncovered oncologic indications. **OUTCOMES ITEMS USED IN THE DECISION:** The main outcomes were change in intended management strategy and whether the PET scan allowed physicians to avoid other tests or procedures. Based on these, Medicare's Evidence Development and Coverage Advisory Committee (MEDCAC) members had to decide how confident they were that PET improves physician decision-making and clinical outcomes, and that the conclusions were generalizable to other cancers, to PET facilities in the general community, and to the Medicare population. **IMPLEMENTATION STRATEGY:** Since CMS did not have the capacity to design and fund a study, the agency partnered with the American College of Radiology and the Academy of Molecular Imaging. The study itself had to be implemented within a short time do to federal regulations. The registry began patient and physician registration in May of 2006. This design was chosen in part because it balanced the desire for access to this service with the goal of generating evidence of reasonable quality that could be used by CMS to make a final coverage determination. **RESULTS:** After the first year, most PET facilities in the United States had signed up to participate in the registry and a huge nationwide sample of data had been collected. The results from this data analysis demonstrate that physicians report a change in intended disease management strategy in about one out of every three cases and that when broken down by disease cancer type and indication, the figure remains fairly constant (Hillner et al. 2008). This evidence was reviewed in August 2008 at a meeting of MEDCAC. Based on these results and the results of a health technology assessment, MEDCAC members were asked to rate their confidence in the clinical utility of PET and the generalizability of the conclusions. The ratings demonstrated that MEDCAC members have limited confidence that PET improves clinical outcomes based on the evidence. Members pointed out that although the results show that physicians often change their intended management plan, there is no way to know if actual management changed and even if it did, it is also not known whether these changes actually lead to better patient outcomes. Still, on January 6, 2009, CMS issued a decision memo stating that there is now sufficient evidence showing that PET improves health outcomes when used for the diagnosis and staging of all previously uncovered cancer types, warranting coverage for these indications. However, CMS does not believe that there is enough evidence demonstrating the clinical utility of PET for monitoring response to treatment and re-staging. Therefore, these indications will still only be covered through the CED policy, likely necessitating the development of a new prospective study. **LESSONS LEARNED:** The case presented above not only demonstrates that CED is operationally and technically possible while abiding to regulatory procedures, it also demonstrates CED can be used to help support research efforts designed to address questions of importance to health care decision-makers. In addition, as this is one of the first examples of Medicare taking advantage of CED, it also offers some lessons for the future. For instance, in order to streamline the process, it is necessary to identify a stable source of funding for these projects, to identify promising technologies which lack evidence of clinical effectiveness earlier in the development process, to reach a shared understanding among stakeholders of standards of evidence that are feasible and sufficiently robust for coverage decisions, and to reach a consensus as to the most efficient methods for conducting real world trials. In the future, it would be best if decisions of study design did not take place while Medicare was making a coverage determination and if private payers became involved in CED so a broader range of patients could participate in the studies.

CASE2

TOWARDS AN INTEGRATED APPROACH TO THE ASSESSMENT OF SURROGATE OUTCOME DATA

Platona A, Lopert R, Sansom L
Department of Health and Ageing, Canberra, ACT, Australia

ORGANIZATION: The Pharmaceutical Benefits Advisory Committee (PBAC) is a statutory independent expert committee which makes recommendations to the Australian Government on medicines to be listed on the national reimbursement formulary (Pharmaceutical Benefits Scheme). **PROBLEM OR ISSUE ADDRESSED:** The proportion of regulatory and reimbursement applications in which the efficacy assessment is limited to surrogate outcome data is increasing. Pressure to bring products to market quickly and facilitate access by patients to new treatments, as well as the costs and time involved in conducting clinical endpoint trials, has led to increasing reliance on these data. While substantial activity is focused on methodological, mainly statistical, approaches to the validation of surrogate outcomes, the determination of the magnitude of absolute or comparative treatment benefit offered by new medicines must be made by regulatory and reimbursement decision makers even where validity has not been clearly demonstrated. **GOALS:** To highlight the need for a more coordinated approach to clinical trial design and the assessment of outcome data by regulatory and reimbursement agencies with respect to reliance on surrogate outcomes. **OUTCOMES ITEMS USED IN THE DECISION: IMPLEMENTATION STRATEGY:** In late 2007, the PBAC established a multidisciplinary working group which included representatives from the PBAC and its Economics Sub-Committee, and the Australian regulator (the Therapeutic Goods Administration), as well as external experts, and representatives of the pharmaceutical industry with the objective of identifying recent developments, policy and methodological, with respect to surrogate outcome data. **RESULTS:** One of the more complex issues encountered during the comparative effectiveness and comparative cost effectiveness assessment of medicines is the determination of the incremental treatment effect when the available evidence is limited to surrogate outcome data. Reimbursement decision-makers attempting to determine incremental cost effectiveness must not only identify any qualitative difference in treatment effect, this must also be measured and valued for incorporation into cost effectiveness analysis. Where clinical benefit is only demonstrated against a surrogate endpoint and where the validity of that surrogate endpoint is uncertain, the relationship between a change in the surrogate and a change in the final clinical endpoint will also be uncertain. Despite much analysis and deliberation the working group was unable to identify a definitive strategy for evaluating a surrogate outcome data in the context of an economic evaluation, but acknowledged that the transformation of surrogates outcomes into final outcomes is associated with significant and extensive uncertainty which can substantively impact on the capacity of decision makers to make robust determinations of comparative cost effectiveness. This difficulty and uncertainty could be reduced through greater, earlier and more systematic collaboration between regulators and funders, and coordinated engagement with the developers of new products. Although formal cooperation agreements exist between a number of regulatory agencies, formal relationships between regulators such as the EMEA and any of the European HTA/reimbursement agencies, such as the UK's National Institute for Health and Clinical Excellence (NICE), for the joint identification, evaluation and validation of surrogate endpoints, and the determination of the significance accorded to them in the regulatory and reimbursement decision-making process, do not appear to exist. **LESSONS LEARNED:** Regulators evaluating medicines for marketing approval processes are not the only decision makers who rely on the results of randomised trials. The commercial success of a new medicine is increasingly dependent on a successful reimbursement approval, and this often means significant public investment. Ideally regulatory-reimbursement collaboration should occur in the design phase of clinical trials so that endpoints that are meaningful, measurable and relevant to both regulators and funders are identified and utilised. Policy makers currently debating the establishment of a framework for comparative effectiveness research in the United States may also wish to engage in the debate around the identification, selection and validation of surrogate endpoints as this will be essential to the meaningful interpretation of these comparative analyses. Overall, the role of multiple decision makers in the process from drug development to drug subsidy and the need for better coordination is a very important one.

CASE3

HEALTH SERVICES PHARMACEUTICAL COVERAGE FOR COMMON DISEASES MAY BE CHALLENGED BY SIGNIFICANT RISE IN ONCOLOGY DRUG EXPENDITURE

Katzir I, Westerman-Landes J, Siegelmann-Danieli N, Kokia E, Lomnicky Y
Maccabi Healthcare Services, Tel Aviv, Israel

ORGANIZATION: Maccabi Healthcare Services. **PROBLEM OR ISSUE ADDRESSED:** Health Care Services face the challenges of accommodating modern therapies in the face of rising costs for newly developed drugs. Maccabi Health Services (MHS) is an leading Israeli health organization known for an early adoption of newly